

What is claimed is:

1. A method for obtaining a disease-associated gene, wherein a disease-associated transcription factor is expressed in a cell line that is deficient in said transcription factor or in a primary cultured cell, and the gene the expression of which is thereby induced or inhibited is screened.

2. A method for obtaining a Runx2/Cbfa1-related disease-associated gene, wherein Runx2/Cbfa1 is expressed in a Runxs/Cbfa1-deficient chondrocyte cell line or in a Runx2/Cbfa1-deficient primary cultured cell, and the gene the expression of which is thereby induced or inhibited is screened.

3. A method for obtaining a gene associated with regulation of cartilage differentiation, wherein Runx2/Cbfa1 is expressed in a Runxs/Cbfa1-deficient chondrocyte cell line or in a Runx2/Cbfa1-deficient primary cultured cell, and the gene the expression of which is thereby induced or inhibited is screened.

4. The method according to any one of claims 1 to 3, wherein said screening is carried out via subtraction or DNA chip analysis.

5. A primary chondrocyte or cultured chondrocyte derived from a Runx2/Cbfa1-deficient mouse.

6. A chondrocyte derived from a Runx2/Cbfa1- and p53-deficient mouse.

7. The chondrocyte cell line derived from the Runx2/Cbfa1- and p53-deficient mouse according to claim 6, which is the RU-1 cell line or the RU-22 cell line deposited under the accession number FERM BP-10137 or FERM BP-10138 at the International Patent Organism Depository of the National Institute of Advanced Industrial Science and Technology.

8. A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, or 25, wherein the expression thereof is induced by Runx2/Cbfa1 expression.

9. A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 9.

10. A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 1 and encoding a protein capable of stimulating cartilage differentiation.

11. A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 3 and encoding a protein capable of inhibiting cartilage differentiation.

12. A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 5 and encoding a protein capable of stimulating cartilage differentiation.

13. A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 15 and encoding a protein capable of inhibiting cartilage differentiation.

14. A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 25 and encoding a protein capable of inhibiting chondrogenesis.

15. A human homolog polynucleotide of the polynucleotide according to claim 8, which has the nucleotide sequence shown in SEQ ID NO: 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, or 51.

16. A polynucleotide having 65% or more homology to the polypeptide encoded by the polynucleotide according to any one of claims 8 to 15, and encoding a protein capable of stimulating or inhibiting cartilage differentiation.

17. A polynucleotide being capable of hybridizing under stringent conditions to the polynucleotide according to any one of claims 8 to 15 or a complementary strand thereof, and encoding a protein capable of stimulating or inhibiting cartilage differentiation.

18. A recombinant DNA vector comprising the polynucleotide according to any one of claims 8 to 17 or a complementary strand thereof.

19. A transformant transformed with the recombinant DNA vector according to claim 18.

20. A polypeptide comprising the amino acid sequence shown in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, or 52.

21. A polypeptide comprising an amino acid sequence derived from the amino acid sequence shown in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26,

28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, or 52 by deletion, substitution, or addition of one or several amino acid residues, and capable of stimulating or inhibiting cartilage differentiation.

22. A polypeptide comprising an amino acid sequence having at least 65% homology to the amino acid sequence shown in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, or 52, and capable of stimulating or inhibiting cartilage differentiation.

23. An antisense polynucleotide which regulates the expression of the gene consisting of the polynucleotide according to any one of claims 8 to 17.

24. An RNAi molecule which regulates the expression of the gene consisting of the polynucleotide according to any one of claims 8 to 17.

25. An antibody against the polypeptide according to any one of claims 20 to 22.

26. A method for screening for a therapeutic agent and/or prophylactic agent for a bone and/or joint disease comprising the following steps (1) to (3):

(1) a step of bringing a candidate compound into contact with a cell that expresses the gene consisting of the polynucleotide according to any one of claims 8 to 17;

(2) a step of assaying the expression level of the gene; and

(3) a step of selecting a compound that lowers or enhances the expression level of the gene compared with a control, which has not been brought into contact with the candidate compound.

27. A method for screening for a therapeutic agent and/or prophylactic agent for a bone and/or joint disease comprising the following steps (1) to (3):

(1) a step of bringing a cell into contact with a candidate compound, wherein a vector containing the transcription regulatory region of the gene consisting of the polynucleotide according to any one of claims 8 to 17 and a reporter gene expressed under the control of the transcription regulatory region has been introduced into the cell;

(2) a step of assaying activity of the reporter gene; and

(3) a step of selecting a compound that lowers or enhances the expression level of the reporter gene compared with a control, which has not been brought into contact with the candidate compound.

28. A method for screening for a therapeutic agent and/or prophylactic agent for a bone and/or joint disease comprising the following steps (1) to (3):

(1) a step of administering a candidate compound to a test animal;

(2) a step of assaying the expression level of the gene consisting of the polynucleotide according to any one of claims 8 to 17 in a biological sample obtained from the test animal; and

(3) a step of selecting a compound that lowers or enhances the expression level of the gene compared with the control to which the candidate compound has not been administered.

29. A method for screening for a therapeutic agent and/or prophylactic agent for a bone and/or joint disease comprising the following steps (1) to (3):

(1) a step of bringing a protein encoded by the gene consisting of the polynucleotide according to any one of claims 8 to 17 into contact with a candidate compound;

(2) a step of assaying activity of the protein; and

(3) a step of selecting a compound that lowers or enhances the activity of the protein compared with a control, which has not been brought into contact with the candidate compound.

30. A compound selected by the screening method according to any one of claims 26 to 29.

31. A pharmaceutical composition comprising at least one of: the polynucleotide according to any one of claims 8 to 17; the DNA vector according to claim 18; the transformant according to claim 19; the polypeptide according to any one of claims 20 to 22; the antisense polynucleotide according to claim 23; the RNAi molecule according to claim 24; the antibody according to claim 25; and the compound according to claim 30.

32. A prophylactic agent and/or therapeutic agent for a bone and/or joint disease comprising at least one of: the polynucleotide according to any one of claims 8 to 17; the DNA vector according to claim 18; the transformant according to claim 19; the polypeptide according to any one of claims 20 to 22; the antisense polynucleotide according to claim 23; the RNAi molecule according to claim 24; the antibody according to claim 25; and the compound according to claim 30.

33. The prophylactic agent and/or therapeutic agent according to claim 32, wherein the bone and/or joint disease is osteoarthritis.

34. A composition for diagnosing a disease comprising at least one of: the polynucleotide according to any one of claims 8 to 17; the DNA vector according to claim 18; the transformant according to claim 19; the polypeptide according to any one of claims 20 to 22; the antisense polynucleotide according to claim 23; the RNAi molecule according to claim 24; the antibody according to claim 25; and the compound according to claim 30.

35. A composition for diagnosing a bone and/or joint disease comprising at least one of: the polynucleotide according to any one of claims 8 to 17; the DNA vector according to claim 18; the transformant according to claim 19; the polypeptide according to any one of claims 20 to 22; the antisense polynucleotide according to claim 23; the RNAi molecule according to claim 24; the antibody according to claim 25; and the compound according to claim 30.

36. The composition according to claim 35, wherein the bone and/or joint disease is osteoarthritis.

37. A transgenic animal model of a bone and/or joint disease, in which an expression level of the gene encoded by the polynucleotide according to any one of claims 8 to 17 is enhanced or lowered.

38. A transgenic mouse model of a bone and/or joint disease, in which the gene encoded by the polynucleotide according to any one of claims 8 to 17 is expressed with the use of a type II collagen promoter.

39. A method for preparing an animal model of a bone and/or joint disease

comprising administering at least one of: the DNA vector according to claim 18; the transformant according to claim 19; the polypeptide according to any one of claims 20 to 22; the antisense polynucleotide according to claim 23; the RNAi molecule according to claim 24; the antibody according to claim 25; and the compound according to claim 30.

40. The method for preparing an animal model according to claim 39, wherein the bone and/or joint disease is osteoarthritis.